Effect of octapeptide of cholecystokinin on canine pyloric pressure

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ISENBERG, JON I., AND ATTILA CSENDES. Effect of octapeptide of cholecystokinin on canine pyloric pressure. Am. J. Physiol. 222(2) : 428-431. 1972.—Intraluminal pressure was measured in five dogs with gastric and duodenal cannulas. Open-tipped perfused tubes were used as pressure sensors. To localize the pylorus (i.e., gastroduodenal junction), transmural potential difference was recorded. The sensors were moved in 1-cm increments, at 15-sec intervals, back and forth across the pylorus. On separate days the C-terminal octapeptide of cholecystokinin (0.25, 0.5, and 1.0 μg/ kg·hr) was infused intravenously. NaCl, 0.15 M, infused alone served as the control. Mean (±se) resting pyloric pressure when the sensors were moved from stomach to duodenum was 14.8 ± 1.0 cm H2O. When they were moved from duodenum to stomach, it was 8.9 ± 0.9 cm H2O. The higher doses of the octapeptide of cholecystokinin (0.5 and 1.0 μg/kg·hr) produced an increase in pyloric pressure. Mean sphincter length was 1.8 cm. It is concluded that the dog pylorus was tonic and that the resting tone was increased by intravenous infusion of the C-terminal octapeptide of cholecystokinin.

GASTRODUODENAL JUNCTION; SPHINCTER; POTENTIAL DIFFERENCE

OPEN-TIPPED PERFUSED TUBES have been shown to be the most accurate sensors for measuring intraluminal spincteric pressure (7). This report describes the manometric characteristics of the canine pylorus (i.e., gastroduodenal junction) using perfused tubes as sensors and describes the effect of the C-terminal octapeptide of cholecystokinin (OP-CCK) on pyloric pressure.

METHODS

Five mongrel dogs, 19-31 kg, were prepared with a Thomas cannula (13) in the stomach 6-8 cm proximal to the gastroduodenal junction, and a second Thomas cannula in the duodenum, 12-15 cm distal to the gastroduodenal junction. Experiments were begun at least 4 weeks after surgery. A No. 3 surgical silk thread was passed from the gastric fistula to the duodenal fistula. This thread remained in place between studies and served to facilitate passage and accurately control the position of the sensors.

Two polyvinyl tubes (id 0.84 mm) perfused with water (0.42 ml/min) by a syringe pump (Harvard Apparatus, Millis, Mass.) were used as sensors. The 1.9-mm oval side openings were separated by a distance of 5 cm. The tubes were attached to pressure transducers (Statham Instruments, model P23BB, Hato Rey, Puerto Rico), and a direct-reading recorder (Sanborn Company, model 267 AC, Wal- tham, Mass.).

To localize the abrupt change in potential difference which occurs at the pylorus (1), a polyethylene tube (id.11 mm) filled with KCl agar was placed next to one of the pressure sensors. Another KCl-agar polyethylene tube (id.06 mm) was placed in a leg vein. Each KCl-agar bridge was placed in a beaker containing saturated KCl and a calomel reference electrode. The reference electrodes were attached to a potentiometer (Radiometer, model PHM 29R, Copenhagen, Denmark), and the direct-writing recorder.

The dogs were fasted for at least 18 hr before each study. The tube assembly was introduced through the gastric fistula. It was moved in 1-cm increments, at 10- to 15-sec intervals, from stomach to duodenum and from duodenum to stomach. Throughout each test NaCl, 0.15 M, was infused intravenously at 30 ml/hr by a peristaltic pump (Harvard Apparatus, Millis, Mass.). After six basal pullthroughs back and forth across the pylorus, the OP-CCK (Squibb Institute for Medical Research, New Brunswick, N. J.) was added to the NaCl infusion, and six more pullthroughs performed. The doses of octapeptide tested were: 0.25, 0.5, and 1.0 μg/kg·hr. NaCl alone served as the control. Each dose was tested once in each of the five dogs. One dose was tested on a single day, and tests were performed twice weekly. Resting gastric antral pressure served as zero reference. Only a sustained (greater than 20 sec) increase in base-line pressure at the gastroduodenal junction was recorded as a zone of increased pressure.

The Student t tests for paired and unpaired values and Chi-squared test were used in the statistical analysis of the data (12).

RESULTS

When the sensors were moved from stomach to duodenum, the mean resting pressure of the gastroduodenal junction (i.e., pyloric sphincter) in the four separate tests (saline control, three OP-CCK tests) ranged from 12.0 to 19.4 cm H2O. Mean resting pressure was calculated by averaging the results of 30 (6 in each of 5 dogs) pullthroughs during the basal period for each separate dose tested. When the sensors were moved from duodenum to stomach, the pressure ranged from 4.2 to 14.1 cm H2O. The zone of increased pressure occurred at the same location, regardless of the direction of the sensors. The mean sphincter pressure was significantly greater (P < 0.01) than the duodenal-to-stomach pressure (Table 1). In addition, there...
was approximately 30 mv (stomach - 25 mv, duodenum, ug/kg-hr), significantly changed pyloric pressure. The larger was recorded by the accompanying potential difference sensor. The change in potential difference across the pylorus occurred at the same time the change in potential difference in either direction of movement of the sensors (Table 1).

In all pullthroughs the pyloric zone of increased pressure had not been previously applied to the canine pylorus. The pressure they recorded by the balloon sensors was greater than that recorded by the unperfused tube sensors. Studies in man, using balloon or nonperfused open-tipped tubes as sensors, have also failed to record a sustained zone of increased pressure at the pylorus when the sensors were moved from duodenum to stomach (1, 2). In dog, Brink, Schlegel, and Code (4), however, recorded a pyloric sphincteric zone when either unperfused open-tipped tubes or small balloons were pulled from duodenum to stomach. The pressure they recorded by the balloon sensors was greater than that recorded by the unperfused tube sensors.

Harris, Pope, and their associates (7, 10, 15) have demonstrated that continuous perfusion of the sensing tube with water produced a more accurate measurement than either nonperfused tube or balloon sensors of both anal and gastroesophageal sphincter strength. The perfused tube technique had not been previously applied to the canine pylorus. The present study demonstrated that there was a zone of increased pressure at the dog gastroduodenal junction. Anderson and Grossman (1), using the transluminal potential difference technique, demonstrated that the gastroduodenal junction coincided with the pyloric sphincter in dogs. The zone of increased pressure was approximately 2 cm in length and increased in tone during an intravenous infusion of the C-terminal octapeptide of cholecystokinin. Intraduodenal fat, a known releaser of cholecystokinin (CCK), and intraduodenal acid, also a releaser of CCK (3), was found by Brink et al. (4) to produce an increase in pyloric pressure in dog.

OP-CCK is several times more potent than CCK on both a weight and molar basis (9). In in vitro and in vivo guinea pig gall bladder 1 µg of OP-CCK is equivalent to approximately 30 Ivy dog units (IDU) or 10 µg of cholecystokinin (1 µg CCK equals approximately 3 IDU). In dogs with chronic pancreatic fistulas, mean peak pancreatic protein secretion was observed during OP CCK 0.5 µg/kg-hr (6). The doses of OP-CCK used in this study therefore were near maximal, maximal, and supramaximal for pancreatic

### Table 1. Basal pyloric pressure

<table>
<thead>
<tr>
<th></th>
<th>Stomach to Duodenum: A</th>
<th>Duodenum to Stomach: B</th>
<th>A vs. B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>116</td>
<td>114</td>
<td></td>
</tr>
<tr>
<td>Pressure, cm H$_2$O</td>
<td>14.8 ± 1.0</td>
<td>8.9 ± 0.9</td>
<td>$P &lt; 0.01$</td>
</tr>
<tr>
<td>Percent 0's</td>
<td>17</td>
<td>39</td>
<td>$P &lt; 0.01$</td>
</tr>
<tr>
<td>Length, cm</td>
<td>1.9 ± 0.1</td>
<td>1.8 ± 0.1</td>
<td>$P &gt; 0.05$</td>
</tr>
</tbody>
</table>

Pressure and length values are means ± se.

#### FIG. 1. Change in mean pyloric pressure during saline control and graded doses of C-terminal octapeptide of cholecystokinin. Each point represents mean of 30 pullthroughs in 5 dogs.

#### FIG. 2. Percent of pullthroughs across pylorus when a zone of increased pressure was recorded during saline control and graded doses of C-terminal octapeptide of cholecystokinin. Each point represents results of 30 pullthroughs in 5 dogs. ZIP refers to zone of increased pressure.
protein secretion. In order to determine whether or not the effect of CCK on the canine pyloric sphincter was a physiologic one, it will be necessary to examine whether the release of endogenous CCK by physiologic methods produces the same effect as did exogenous OP-CCK. Because CCK (GIH Laboratory, Karolinska Institute, Stockholm, Sweden) contains approximately 90% impurities (8), it was decided to use the pure synthetic OP-CCK for this study.

We do not know why the pyloric pressure was greater when the sensors were moved from stomach to duodenum.
CHOLECYSTOKININ ON CANINE PYLORIC PRESSURE

than when they were moved from duodenum to stomach. Possible explanations include: a duodenal neural reflex which was stimulated when the sensors were pulled from stomach to duodenum, and not stimulated when the sensors were moved from duodenum to stomach; or movement of the gastric mucosa into the pyloric sphincteric area while the sensors were pulled into the duodenum, thereby decreasing the effective size of the sphincter.

REFERENCES